

REMARKS

Amendments to the Specification, Drawings, and Sequence Listing:

Figures 1A-C and SEQ ID NOS:1 and 2 have been amended to correct minor errors in these sequences, as shown in red ink in the marked-up version of original Figures 1A-C, submitted herewith (at Tab 2). Accordingly, Applicants submit herewith substitute sheets of Figures 1A-C (at Tab 1) and a Substitute Sequence Listing which correct the errors in the sequence shown in original Figures 1A-C and original SEQ ID NOS:1 and 2. The specification has been amended at page 4 and Figures 2 and 3 have been canceled to reflect these amendments to the sequences. The amendments to these sequences introduce no new matter.

Applicants note that Figures 1A-C as originally filed in the instant application contain three typographical errors in specific nucleotides, that were, however, correctly disclosed in original Figures 1A-C of prior Application No. 08/459,101, which was incorporated by reference in the instant application by way of the Preliminary Amendment filed concurrently with the instant application. For the Examiner's convenience, a copy of original Figures 1A-C of prior Application No. 08/459,101 is attached hereto at Tab 3. These three particular nucleotides that are typographical errors in original Figures 1A-C are each marked with an asterisk (*) in the marked-up copy of original Figures 1A-C at Tab 2 hereto.

With respect to the additional corrections, the cDNA of the disclosed clone of ATCC deposit number 75804 inherently contains the corrected nucleotide sequence set forth in SEQ ID NO:1 of the Substitute Sequence Listing and of substitute Figures 1A-C, and, thus, inherently encodes the amino acid sequence set forth in SEQ ID NO:2 of the Substitute Sequence Listing and of substitute Figures 1A-C. There is a line of case law in which applicants have been permitted to amend the specification to correct the formula of a chemical compound after an application's filing date, provided that it had been demonstrated that one of skill in the art would have appreciated that the applicants were in possession of the compound itself at the time of filing. The rationale is that the formula is an inherent property of the compound and, thus, amending the specification to correct the new formula is not new matter. *See, In re Nathan*, 328 F.2d 1005, 1008, 140 U.S.P.Q. 601, 604 (C.C.P.A. 1964); *accord Kennecott Corp. v. Kyocera Int'l, Inc.*, 5 U.S. P.Q.2d 1194, 1198 (Fed. Cir. 1987), *cert denied*, 486 U.S. 1008 (1988) ("The disclosure in a subsequent patent application of an inherent property of a product does not deprive that product of the benefit of the earlier filing date"). The standard applied in *Nathan* was whether the original specification discloses the claimed

compounds and provides "the means for identifying them irrespective of the wrong formulae."
Nathan, 328 F.2d at 1008.

To expedite prosecution, Applicants submit herewith an executed Declaration Of Donna Dimke Under 37 C.F.R. § 1.132 ("Dimke Declaration") setting forth the required facts to demonstrate that the corrections of the sequences set forth in Figures 1A-C and SEQ ID NOS:1 and 2 introduce no new matter. As the Dimke Declaration shows, the clone contained in ATCC deposit number 75804, as disclosed in the instant application, was obtained from the ATCC and re-sequenced using original Figures 1A-C of prior Application No. 08/459,101 as a guide (Dimke Declaration, ¶¶ 2-3). As shown in the marked-up version of original Figures 1A-C, of the 1,146 nucleotides of the correct nucleotide coding sequence of the cDNA clone of ATCC Deposit Number 75804, original Figures 1A-C of the instant application had 1,113 identical nucleotides; and of the 381 amino acids of the correct amino acid sequence encoded by the cDNA clone of ATCC Deposit Number 75804, original Figures 1A-C of the instant application had 359 identical amino acids. See Dimke Declaration, ¶ 4. Thus, as Ms. Dimke stated in her Declaration, the correct nucleotide and encoded amino acid sequence for ATCC deposit number 75804, which is shown in the corrected version of Figures 1A-C submitted herewith, would be readily obtained with only routine experimentation upon sequencing the cDNA of ATCC deposit number 75804, particularly when using original Figures 1A-C of prior Application No. 08/459,101 as a guide (Dimke Declaration, ¶ 5). Therefore, the instant specification as filed provides the means for identifying the correct sequence of the claimed polynucleotides and specified polypeptides irrespective of the incorrect sequence in original Figures 1A-C.

Clearly, the discrepancies between the originally disclosed sequence of the Connective Tissue Growth Factor-2 (CTGF-2) polypeptide of the invention are so insignificant that the description of the CTGF-2 cDNA and encoded polypeptide sufficiently distinguished these molecules from others, *i.e.*, there would be no question that the Applicants described the genus of claimed molecules. See *Nathan*, 328 F.2d at 1008. In other words, like the original CTGF-2 sequence, one skilled in the art would readily recognize the correct CTGF-2 sequence as having homology to the mouse CTGF protein and Cyr61 protein as described in the specification at page 4, while still being distinct from these as well as all other previously known proteins. Indeed, the specification states that the CTGF-2 protein of the instant invention is "a member of an emerging family of cysteine-rich secreted proteins that includes connective tissue growth factor..." (sentence bridging pages 4-5 of the specification). Applicants particularly note that none of the many cysteine

residues in original Figures 1A-C and SEQ ID NO:2 required correction. Therefore, as in *Nathan*, the amendments to the sequences set forth above introduce no new matter.¹

Statements Under 37 C.F.R. § 1.825(a) And (b)

Pursuant to 37 C.F.R. § 1.825(a), the undersigned attorney for Applicants hereby states that the Substitute Sequence Listing submitted herewith is completely supported by the specification as filed and no new matter has been introduced. Specifically, the amendments to SEQ ID NOS:1 and 2 contained in the Substitute Sequence Listing are inherent features of the disclosed cDNA of ATCC deposit number 75804, whose sequence was disclosed, with minor errors, in original Figures 1A-C, as detailed above (and with even fewer minor errors, as detailed above, in original Figures 1A-C of prior Application No. 08/459,101).

Pursuant to 37 C.F.R. § 1.825(b), the undersigned attorney for Applicants hereby states that the information contained in the computer readable copy of the Substitute Sequence Listing, submitted herewith, is identical to the information contained in the computer readable copy of the Substitute Sequence Listing, submitted herewith.

Amendments to the Claims:

Claim 1 and 21-97 are currently pending in light of the amendments above. Claims 2-20 have been canceled without prejudice and Applicants reserve the right to pursue the subject matter of these claims in this or related applications. New claims 21-97 correspond to Group II which Applicants provisionally elected in the Provisional Election filed on September 29, 2000, in response to the Restriction Requirement mailed on March 31, 2000. Claims 21-97 have been added to more particularly point out an distinctly claim the subject matter that Applicants regard as the invention. The claims are completely supported in the specification as originally filed and no new matter has been introduced. More specifically, support can be found, for example, at page 10, third full paragraph (full-length polypeptide), page 17, lines 1-2 (polypeptides lacking the N-terminal

¹ Moreover, the instant case is quite distinguishable from the situation in *Ex parte Maizel*, 27 U.S.P.Q.2d 1662 (B.P.A.I. 1992), in which the board found that correction of nucleotide sequences is indeed proper in some cases. In *Maizel*, however, the applicants had failed to demonstrate that the re-sequenced clone was the same as the clone deposited with the ATCC. In addition, the board found that the DNA had been "badly misdescribed" because a frame shift in the middle of the coding sequence was alleged to have altered the starting position and a significant portion of the N-terminus of the deduced polypeptide sequence, in a manner the board found unclear, such that "the amino acid content of the [corrected] protein differs dramatically." *Id.* In contrast, in the instant case, Ms. Dimke resequenced the very

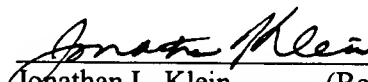
methionine), page 4, last two paragraphs (mature polypeptide), page 9, first three paragraphs (fragments), page 1, second paragraph; page 3, first paragraph; and page 17, second and third full paragraphs (stimulating cellular proliferation), page 10, first full paragraph (at least 30 contiguous amino acids; at least 50 contiguous amino acids; at least 90% identity; at least 95% identity), the sentence bridging pages 14-15 (heterologous polypeptides).

Conclusion

Applicants respectfully request that the amendments and remarks above, including the provisional election with traverse, be entered and made of record in the file history of the instant application.

Respectfully submitted,

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deposited clone that was disclosed in the instant specification as filed, by ATCC deposit number; and only a few amino acids required correction with no modification or adjustment of the N-terminus (Dimke Declaration, ¶¶ 2-5).